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Nanoscopy for nanomedicine group

Group leader: Lorenzo Albertazzi (lalbertazzi@ibecbarcelona.eu)

Combining super resolution and electron microscopy to track nanoparticles inside the cell

Nanomaterials hold a great promise for a variety of biomedicine applications, with a special focus on drug delivery for cancer therapy. In the development of successful therapies, it is crucial to understand the transport of nanoparticles inside the cell. However, tracking nanoparticles intracellularly has been challenging due to the diffraction limit in conventional optical microscopes: nanoscale was unreachable, thus single nanoparticles could not be observed.

In the recent years super resolution microscopy (SRM) has emerged as a very powerful tool able to surpass the diffraction limit and reach the nanoscale. Since it won the Nobel Prize in 2014 it has been mainly used for cell biology and it has yet to be fully exploited for nanomedicine. We believe it is the perfect technique to study the transport of nanoparticles inside the cell. However, as with classical light microscopy, SRM does not provide information on the subcellular context of the molecule, the "reference space" (cellular ultrastructure), is still lacking.

On the other hand, electron microscopy (EM) is a powerful imaging technique as its high spatial resolution (in the order of few nanometers) allows for a detailed observation of cellular structures. However, while visualizing specific molecules by light microscopy is easily performed by labelling with a fluorescent tag, in EM it is still challenging. Thus, we want to combine both techniques: SRM for molecule specific imaging and EM to visualize the different cellular organelles. Both techniques together will be much more powerful and shed light about nanoparticle's internalization process (1+1=3).

There have been very few attempts to combine SRM and EM but none exists for nanomaterials, thus its development will strongly impact the field of nanomaterials providing a valuable tool for the whole community of chemistry and materials working towards biomedical applications.

Job position description

The student will be involved in:

- 1) Modification of nanoparticles with functional ligands for cancer recognition and dyes for imaging; study nanoparticle cellular internalization.
- 2) Learning the use of super resolution microscopy for tracking nanomaterials in cancer cells.
- 3) Learning the use of electron microscopy to get the cellular "reference space".
- 4) Development of the method to combine both methodologies and get enhanced information on the precise localization of nanoparticles inside the cell.
- 5) The biological evaluation of the nanoparticles efficacy for drug delivery and cancer therapy, allowing the design of improved nanoparticles. The project is in the framework of several European consortia and collaborations and visiting period abroad are envisioned.